



Docket No. NB 2017

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Pursuant to 37 C.F.R. § 1.8, I hereby certify that this paper and all enclosures are being deposited with the United States Postal Service as first class mail on the date indicated below in an envelope addressed to the Commissioner for Patents, Washington D.C. 20231.

[ ] Pursuant to 37 C.F.R. § 1.6(d), I hereby certify that this paper and all enclosures are being sent via facsimile on the date indicated below to the attention of the Commissioner for Patents at Facsimile No. (703) 872-9306 at \_\_\_\_\_ a.m./p.m.

Dated: April 16, 2002

Name of Person Certifying: Jocelyn L. Lee

Printed Name: Jocelyn L. Lee

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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application for:

H. Michael SHEPARD, et al.

Serial No.: 09/910,345

Filing Date: July 20, 2001

For: **METHODS FOR IDENTIFYING  
THERAPEUTIC TARGETS FOR  
TREATING INFECTIOUS DISEASE**

Examiner: Not Yet Assigned

Group Art Unit: 1645

Commissioner for Patents  
Washington, D.C. 20231

**INFORMATION DISCLOSURE STATEMENT**

Sir:

In accordance with 37 C.F.R. § 1.56, the references listed on the attached Form PTO-1449 are being brought to the attention of the Examiner for consideration in connection with the examination of the above-identified patent application.

**I. Timing of the Information Disclosure Statement:**

This Information Disclosure Statement is filed:

- ☐ With the new patent application submitted herewith (37 C.F.R. § 1.97(a)).
- ☐ Within three months after the filing date of the application or within three months after the date of entry of the national stage of a PCT application as set forth in 37 C.F.R. § 1.491.
- ☒ Before the mailing date of a first Office action on the merits. In the event, however, that an Office Action has crossed in the mail with this Information Disclosure Statement, the Commissioner is hereby authorized to charge Deposit Account No. 50-1189 for any fees required pursuant to 37 C.F.R. §§ 1.17(p) or 1.17(i)(1).

This Information Disclosure Statement is filed:



☐ After the first Office Action and more than three months after the application's filing date; or PCT national stage date of entry filing but, as far as is known to the undersigned, prior to the mailing date of either a final rejection or a notice of allowance, whichever occurs first, and the Commissioner is hereby authorized to charge Deposit Account No. [ ] for the fee (\$180) set forth in 37 C.F.R. § 1.17(p) and any additional required fees.

This Information Disclosure Statement is filed:

- ☐ After the mailing date of either a final rejection or a notice of allowance, whichever occurred first, and is accompanied by the fee (\$180.00) set forth in 37 C.F.R. § 1.17(i)(1) and a certification as specified in 37 C.F.R. § 1.97(e), as checked below. This document is to be considered as a petition requesting consideration of the Information Disclosure Statement.

The undersigned certifies that:

- ☐ Each item of information contained in the Information Disclosure Statement was first cited in any communication mailed from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this information disclosure statement.
- ☐ No item of information contained in this information disclosure statement was cited in a communication mailed from a foreign patent office in a counterpart foreign application or, to the knowledge of the undersigned after making reasonable inquiry, was known to any individual designated in 37 C.F.R. § 1.56(c) more than three months prior to the filing of this Information Disclosure Statement.

## II. Copies of the Cited Items:

- ☒ Copies of all of the items listed on the attached Form PTO-1449 are enclosed.
- ☐ Copies of only the following items listed on the attached Form PTO-1449 are enclosed: \_\_\_\_\_.
- ☐ Copies of those items listed in the attached Form PTO-1449 are not supplied because they were previously cited by or submitted to the Patent Office in a prior Application No. 09/516,488, filed March 1, 2000 and relied upon in this application for an earlier filing date under 35 U.S.C § 120. See 37 C.F.R. § 1.98(d).
- ☐ Copies of those items which are marked with an asterisk (\*\*) in the attached Form PTO-1499 were cited in a foreign examination report in a related case. A copy of the search report and the cited references not already of record in this application are attached hereto.

### III. Concise Explanation of Relevance:



A concise explanation of relevance of the items listed on Form PTO-1449 is not given.

A concise explanation of relevance of [some of] the items listed on Form PTO-1449 is in the form of an English language copy of a Search Report from a foreign patent office, issued in a counterpart application, which refers to the relevant portions of the references (copy attached).

### IV. Conclusion:

Citation of the above documents shall not be construed as:

1. an admission that the documents are necessarily prior art with respect to the instant invention;
2. a representation that a search has been made, other than as described above; or
3. an admission that the information cited herein is, or is considered to be, material to patentability as defined in § 1.56(b).

It is respectfully requested that the Examiner indicate consideration of the cited references by returning a copy of the attached form PTO 1449 with initials or other appropriate marks.

The Commissioner is hereby authorized to charge Deposit Account No. 50-1189, Billing Reference No. 23896-7101 for any additional fees required in connection with the filing of this Information Disclosure Statement.

DATE: April 16, 2002

Respectfully submitted,

By: Antoinette F. Konski

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

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Sheet	1	of	1
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*Complete if Known*

<b>Application Number</b>	<b>09/910,345</b>
<b>Filing Date</b>	<b>July 20, 2001</b>
<b>First Named Inventor</b>	<b>H. Michael Shepard, et al</b>
<b>Art Unit</b>	<b>1645</b>
<b>Examiner Name</b>	<b>Not Yet Assigned</b>
<b>Attorney Docket Number</b>	<b>NB 2017.00</b>

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## U.S. PATENT DOCUMENTS

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## FOREIGN PATENT DOCUMENTS

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# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 1 of 3

Complete if Known

Application Number	09/910,345
Filing Date	July 20, 2001
First Named Inventor	H. Michael Shepard, et al.
Art Unit	1645
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2017.00

## OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published
	1	AMYES, S.G. et al. (1992) "Classification of plasmid-encoded dihydrofolate reductases conferring trimethoprim resistance." <i>J. Med. Microbiol.</i> 36:1-3.
	2	ARTHUR, Michel, et al. (August 1999) "Moderate-Level Resistance to Glycopeptide LY333328 Mediated by Genes of the <i>vanA</i> and <i>vanB</i> Clusters in Enterococci" <i>Antimicrobial Agents and Chemotherapy</i> 43(8):1875-1880.
	3	AULABAUGH, Ann, et al. (1990) "Oxalyl Hydroxamates as Reaction-Intermediate Analogues for Ketol-Acid Reductoisomerase." <i>Biochemistry</i> 29(11):2824-2830.
	4	BERGER-BÄCHI, Brigitte, et al. (1989) " <i>FemA</i> , a host-mediated factor essential for methicillin resistance in <i>Staphylococcus aureus</i> : Molecular cloning and characterization" <i>Mol. Gen. Genet.</i> 219:263-269.
	5	BLIGHT, Keril J., et al. (1998) "Molecular virology of hepatitis C virus: an update with respect to potential antiviral targets" <i>Antivir. Ther.</i> 3(Suppl 3):71-81.
	6	BLOOMER, James L., et al. (1976) "Microbial Metabolites. Part XI. Total Synthesis and Absolute Configuration of (S)-Carlosic Acid (4-Butyryl-2,5-dihydro-3-hydroxy-5-oxo-furan-2-acetic Acid) and Conversion of (R)-5-Methyltetriconic Acid into (R)-Carolic Acid {3,4-Dihydro-8-methylfuro[3,4-b]oxepin-5,6(2H,8H)-di-one}" <i>J. Chem. Soc., Perkin Trans. I</i> 14:1485-1491.
	7	BOHACEK, Regine S, et al. (1997) "Modern computational chemistry and drug discovery: structure generating programs" <i>Curr. Opin. Chem. Biol.</i> 1:157-61.
	8	BONOMO, Robert A., et al. (May 15, 1999) "Inhibitor Resistant Class A Beta-Lactamases" <i>Front Biosci.</i> 4:34-41.
	9	CACERES, Nancy E., et al. (August 1997) "Overexpression of the D-Alanine Racemase Gene Confers Resistance to D-Cycloserine in <i>Mycobacterium smegmatis</i> ." <i>J. Bacteriol.</i> 179(16):5046-5055.
	10	CARLSEN, Per H.J., et al. (1981) "A Greatly Improved Procedure for Ruthenium Tetraoxide Catalyzed Oxidations of Organic Compounds." <i>J. Org. Chem.</i> 46:3936-3938.
	11	CASADEWALL, Barbara, et al. (June 1999) "Characterization of the <i>vanD</i> Glycopeptide Resistance Gene Cluster from <i>Enterococcus faecium</i> BM4339." <i>J. Bacteriol.</i> 181(12):3644-3648.
	12	CASADO, Jose L., et al. (2000) "Non-nucleoside reverse transcriptase inhibitor resistance among patients failing a nevirapine plus protease inhibitor-containing regimen" <i>AIDS</i> 14(2):F1-F7.
	13	CHANG, Alan K., et al. (1998) "Herbicide-resistant forms of <i>Arabidopsis thaliana</i> acetohydroxyacid synthase: characterization of the catalytic properties and sensitivity to inhibitors of four defined mutants" <i>Biochem. J.</i> 333: 765-777.
	14	CHIPMAN, David, et al. (1998) "Biosynthesis of 2-aceto-2-hydroxy acids: acetolactate synthases and acetohydroxyacid synthases" <i>Biochim. Biophys. Acta</i> 1385:401-419.
	15	COHEN, Noal, et al. (1983) "Enantiospecific Syntheses of Leukotrienes C <sub>4</sub> D <sub>4</sub> and E <sub>4</sub> and [14, 15- <sup>3</sup> H <sub>2</sub> ] Leukotriene E <sub>4</sub> Dimethyl Ester." <i>J. Am. Chem. Soc.</i> 105:3661-3672.
	16	DEGRAW, Joseph I., et al. (January-February 1986) "Synthesis of 5,10-Dideazaminopterin." <i>J. Heterocyclic Chem.</i> 23:1-4.
	17	DÖTZ, K.H. (1999) "Reactions of complex ligands 85: chiral quinoid and hydroquinoid [2.2]metacyclophanes via chromium-mediated intramolecular benzannulation." <i>J. Organomet Chem.</i> 578:223-228.
	18	EKINS, Sean, et al. (1999) "Three and four dimensional-quantitative structure activity relationship (3D/4D-QSAR) analyses of CYP2D6 inhibitors." <i>Pharmacogenetics</i> 9:477-489.
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	20	EVANS, M. E., et al. (1667) "Acetal Exchange Reaction" <i>Carbohydrate Res.</i> 3:453-462.

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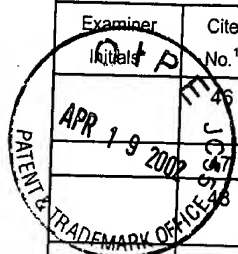
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# OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published
APR 19 2002 PATENT & TRADEMARK OFFICE		FREER, Andrew A., et al. (1996) "Synthesis and absolute configurations of the naturally occurring 3- and 4-methylmuconolactones: X-ray structures of (S)-1-phenylethylammonium salts and an 8-bromo-1-methylmuconodilactone" <i>J. Chem. Soc. Perkin Trans. 1</i> 17:2111-2116.
		GYPSEER, Andreas, et al. (1997) "D-Erythronolactone as a C <sub>4</sub> building unit. Part 2. A short and efficient synthesis of both enantiomers of eip-muricatacin, a diastereoisomer of the native acetogenin from <i>Annona muricata</i> ." <i>Chem. Soc. Perkin Trans. 1</i> , p.1013-1016
	23	GYPSEER, Andreas, et al. (1994) "D-Erythronolactone and 2,3-O-Isopropylidene-L-erythrose as C <sub>4</sub> Building Units: An Efficient Synthesis of both Enantiomers of <i>endo</i> -Brevicommin and its 7-Vinyl Analogues" <i>Liebigs. Ann. Chem.</i> , 775-780.
	24	HALGAND, Frédéric, et al. (1999) "Characterization of the Conformational Changes of Acetohydroxy Acid Isomeroeductase Induced by the Binding of Mg <sup>2+</sup> Ions, NADPH, and a Competitive Inhibitor <sup>1†</sup> " <i>Biochemistry</i> 38:6025-6034.
	25	HANAKI, H., et al. (1998) "Activated cell-wall synthesis is associated with vancomycin resistance in methicillin-resistant <i>Staphylococcus aureus</i> clinical strains Mu3 and Mu50" <i>J. Antimicrob. Chemother.</i> 42(2):199-209.
	26	HANESSIAN, Stephen, et al. (1983) "Total synthesis of the C-3 – C-17 segment of boromycin" <i>Can. J. Chem.</i> 61:634-637.
	27	HARMS, Christian T., et al. (1992) "Herbicide resistance due to amplification of a mutant acetohydroxyacid synthase gene." <i>Mol. Gen. Genet.</i> 233:427-435.
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	29	IBDAH, Muhammad, et al. (1996) "Homology Modeling of the Structure of Bacterial Acetohydroxy Acid Synthase and Examination of the Active Site by Site-Directed Mutagenesis" <i>Biochemistry</i> 35:16282-16291.
	30	KIRKPATRICK, Lynn D., et al. (1999) "Structure-Based Drug Design: Combinatorial Chemistry and Molecular Modeling" <i>Comb. Chem. High Throughput Screen</i> 2:211-221.
	31	KLEANTHOUS, Colin, et al. (1985) "3-(Bromoacetyl)chloramphenicol, an Active Site Directed Inhibitor for Chloramphenicol Acetyltransferase" <i>Biochemistry</i> 24:5307-5313.
	32	LACKEY, David B., et al. (2001) "Enzyme-catalyzed therapeutic agent (ECTA) design: activation of the antitumor ECTA compound NB1011 by thymidylate synthase" <i>Biochem. Pharmacol.</i> 61:179-189.
	33	LESSARD, Ivan A. D., et al. (1999) "Determinants for Differential Effects on D-Ala-D-Lactate vs D-Ala-D-Ala Formation by the VanA Ligase from Vancomycin-Resistant Enterococci" <i>Biochemistry</i> 38:14006-14022.
	34	LEWBART, Marvin L., et al. (November 1969) "Preparation and Properties of Steroidal 17,20- and 20,21-Acetonides Epimeric at C-20. I. Derivatives of 5β-Pregnan-3α-ol" <i>J. Org. Chem.</i> 34(11):3505-3512.
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	36	MALIK, Arshad, et al. (May 2, 2000) "Chronic Hepatitis B Virus Infection: Treatment Strategies for the Next Millennium" <i>Ann. Intern. Med.</i> 132(9):723-731.
	37	MCGOWAN, Donald A., et al. (1982) "Total Synthesis of Racemic Chorismic Acid" <i>J. Am. Chem. Soc.</i> 104:1153-1154.
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	40	MDLULI, Khisimuzi, et al. (1998) "Mechanisms involved in the intrinsic isoniazid resistance of <i>Mycobacterium avium</i> ." <i>Molecular Microbiology</i> 27(6):1223-1233.
	41	MIESEL, Lynn, et al. (1998) "Mechanisms for isoniazid action and resistance" <i>Novartis Found. Symp.</i> 217:209-220.
	42	PANG, Siew Siew, et al. (1999) "Expression, Purification, Characterization, and Reconstitution of the Large and Small Subunits of Yeast Acetohydroxyacid Synthase" <i>Biochemistry</i> 38:5222-5231.
	43	PATRICK, Timothy B., et al. (1994) "New Fluorobutenolide Templates for Synthesis" <i>J. Org. Chem.</i> 59:1210-1212.
	44	PIRRUNG, Michael C., et al. (1991) "Mechanism and Stereochemistry of α,β-Dihydroxyacid Dehydratase" <i>J. Am. Chem. Soc.</i> 113:1020-1025.
	45	POULSEN, Charlotte, et al. (1989) "Purification and properties of <i>Saccharomyces cerevisiae</i> acetolactate synthase from recombinant <i>Escherichia coli</i> " <i>Eur. J. Biochem.</i> 185:433-439.

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# OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS



Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published
	46	RAYNAUD, Catherine, et al. (1999) "Mechanisms of pyrazinamide resistance in mycobacteria: importance of lack of uptake in addition to lack of pyrazinamidase activity" <i>Microbiology</i> 145:1359-1367.
		READ, Timothy D., et al. (September 2001) "Finding drug targets in microbial genomes." <i>DDT</i> 6(17):887-892.
		SHAW, Karen J. et al. (March 1980) "Salmonella typhimurium Mutants Defective in Acetohydroxy Acid Synthases I and II" <i>J. Bacteriol.</i> 141(3):1258-1263.
	49	SHAW, William V., et al. (1988) "Tinkering with antibiotic resistance: chloramphenicol acetyltransferase and its substrates" <i>Biochem. Soc. Trans.</i> 16:939-942.
	50	SHAW, W., et al. (1991) "Chloramphenicol Acetyltransferase" <i>Annu. Rev. Biophys. Biophys. Chem.</i> 20:363-86.
	51	STASCHKE, Kirk A., et al. (1995) "Molecular Basis for the Resistance of Influenza Viruses to 4-Guanidino-Neu5Ac2en." <i>Virology</i> 214:642-646.
	52	SVENDSEN, Axel, et al. (1975) "Naturally Occurring Lactones and Lactams. VIII. Lactonization of Unsaturated $\beta$ -Keto Esters. Total Synthesis of Caric Acid, Carlosic Acid, and Viridicatic Acid" <i>J. Org. Chem.</i> 40(13):1927-1932.
	53	TAKABATAKE, Tohru, et al. (1992) "Bacteriostatic Effect of 4,7-Dicyanobenzofurazan Due to Inactivation of 2,3-Dihydroxyisovalerate Dehydratase" <i>Chem. Pharm. Bull.</i> 40(6):1644-1646.
	54	TETTELIN, Hervé et al. (July 20, 2001) "Complete Genome Sequence of a Virulent Isolate of <i>Streptococcus pneumoniae</i> " <i>Science</i> 293:498-506.
	55	VAGHEFI, Morteza M., et al. (1986) "Synthesis and Antiviral Activity of Certain Nucleoside 5'-Phosphonoformate Derivatives" <i>J. Med. Chem.</i> 29:1389-1393.
	56	VANRHEENEN, V., et al. (1976) "An Improved Catalytic OsO <sub>4</sub> Oxidation of Olefins to <u>CIS</u> -1, 2-Glycols Using Tertiary Amine Oxides as the Oxidant" <i>Tetrahedron Letters</i> 23:1973-1976.
	57	VARGHESE, Joseph N, et al. (1998) "Drug design against a shifting target: a structural basis for resistance to inhibitors in a variant of influenza virus neuraminidase" <i>Structure</i> 6(6):735-746.
	58	VENTURI, Guilietta, et al. (2000) "Antiretroviral Resistance Mutations in Human Immunodeficiency Virus Type 1 Reverse Transcriptase and Protease from Paired Cerebrospinal Fluid and Plasma Samples" <i>J. Infect. Dis.</i> 181:740-745.
	59	VOLLMER, Martin Dominik, et al. (July 1994) "Inability of Muconate Cycloisomerases to Cause Dehalogenation during Conversion of 2-Chloro- <i>cis,cis</i> -Muconate" <i>J. Bacteriol.</i> 176(14):4366-4375.
	60	VOLLMER, Martin Dominik, et al. (May 1995) "Conversion of 2-Chloro- <i>cis,cis</i> -Muconate and Its Metabolites 2-Chloro- and 5-Chloromuconolactone by Chloromuconate Cycloisomerases of pJP4 and pAC27" <i>J. Bacteriol.</i> 177(10):2938-2941.
	61	VOLLMER, Martin Dominik, et al. (September 1998) "Substrate Specificity of and Product Formation by Muconate Cycloisomerases: an Analysis of Wild-Type Enzymes and Engineered Variants." <i>Appl. Environ. Microbiol.</i> 64(9):3290-3299.
	62	WEINSTOCK, Orna, et al. (September 1992) "Properties of Subcloned Subunits of Bacterial Acetohydroxy Acid Synthases" <i>J. Bacteriol.</i> 174(17):5560-5566.
	63	WHITCOMB, Carl E. (1999) "An introduction to ALS-inhibiting herbicides" <i>Toxicol. Ind. Health</i> 15:231-239.
	64	YUAN, Ying, et al. (July 1995) "Identification of a gene involved in the biosynthesis of cyclopropanated mycolic acids in <i>Mycobacterium tuberculosis</i> " <i>Proc. Natl. Acad. Sci. USA.</i> 92:6630-6634.
	65	ZHDANOV, Yu. A., et al. (August 1971) "Reformatsky Reaction in the Carbohydrate Series" <i>Zh. Obshch. Khim</i> 41(8):1845-1847.

Examiner's Signature	Date Considered
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\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

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